Assessing Persistence in Spatial Clustering of Disease, with an Application to Drug Related Deaths in Scottish Neighbourhoods

Peter Congdon

Peter Congdon, School of Geography, Queen Mary University of London United Kingdom - email: p.congdon@qmul.ac.uk

***DOI:* 10.2427/13225**
Accepted on December 13, 2019

ABSTRACT

Background: The upward trend in drug related deaths in some countries is a major public health concern. Regarding geographic location within countries, many studies report spatial clustering in drug related deaths. We consider drug related deaths in Scottish small areas, and investigate probabilities that clusters of adjacent neighbourhoods have elevated risk. We focus especially on assessing persistence in spatial clustering, relevant to prioritising area based interventions. We assess impacts of area risk factors on drug deaths, finding a strong link to poverty, and a clear overlap between drug death clustering and spatial poverty clustering.
Methods: We analyse drug related deaths in 1279 Scotland neighbourhoods over two periods, 2009-13 and 2014-18, during which drug related mortality in Scotland has more than doubled. A fully Bayesian approach is used to identify zones with high mortality risk in both a neighbourhood and its spatial lag ("high-high" clusters), and extended to identify recurring high risk clustering over more than one period. Estimation of mortality risks, and of cluster probabilities through periods, is developed in conjunction with a regression model including area risk factors such as deprivation.
Results: Persistent clustering is concentrated in major urban centres, for example, Glasgow and Dundee. Deprivation is the paramount observed risk factor underlying elevated mortality risk, and persistent clustering in drug related mortality shows strong overlaps with poverty clustering. Social fragmentation modifies the paramount influence of poverty on drug mortality risk.
Conclusion: Cluster persistence is a central feature in small area variability in drug related death risk in Scotland intermediate zones, especially in some urban areas.

INTRODUCTION

There are increasing policy and treatment concerns regarding upward trends in drug-related deaths (DRD) in certain developed societies, including the US and the countries constituting the UK [1]. For example, in the US drug related deaths have nearly doubled, from 36450 in 2008, to 70237 in 2017, and are a major cause of an increase in premature mortality [2]. In the USA drug deaths have an unequal spatial distribution, with clustering apparent, so increasing the burden in some areas relative to others [3,4]. Scotland has similarly undergone a major increase in such

deaths over recent years, exceeding the rate of increase in the US. Scotland now has the highest level of drug related mortality in Europe (218 per million), and a higher rate than the US (217 per million). Regarding spatial aspects of this trend, the most recent official publication on Scottish drug deaths found evidence [5, page 26] of small area geographic concentrations (albeit for 2000-07).

In this paper, we consider spatial variability in drug related mortality over 1279 intermediate zones in Scotland, these zones encompassing the entire nation of Scotland. We focus especially on the upward trend in drug related deaths in Scotland over the last decade, during which such deaths more than doubled, up from 545 deaths in 2009, to 1187 in 2018. We compare the sub-periods 2009-13 and 2014-18, in which there were respectively 2722 and 4309 drug related deaths, with drug related deaths particularly increasing in the latter period.

The fundamental aim of the analysis is to identify spatial clusters with high or low drug mortality risk, and to assess persistence in such clustering through time. An adaptation of the LISA (Local Indicator of Spatial Association) clustering approach is used [6], focusing on obtaining the probability of persisting "high-high" clusters and "low-low" clusters. Such clusters are defined by excess or diminished risk in both individual neighbourhoods and in their spatial lag (the set of adjacent areas). The probabilities that an area is the core of a high-high or low-low cluster are obtained using Markov chain Monte Carlo (MCMC) methods and fully Bayesian inference.

Many studies show strong associations between drug-related deaths and area poverty, due both to contextual influences and reflecting composition of area populations. We therefore aim to show associations between drug deaths and area socio-economic characteristics, including, but not limited to, poverty, as these will have an impact on persistent clustering. Although poverty is of central importance as an area risk factor, impacts of poverty may be modified by social cohesion, and by area type (e.g. urban vs. rural). We also investigate the overlap between spatial cluster persistence in drug-related deaths and clustering persistence in poverty. A final objective is to compare cluster persistence in drug deaths between health agencies, as is relevant for assessing drug treatment needs or other interventions. For example, Mclafferty [7] mentions that "For policymakers and planners, selectively targeting interventions to hotspot areas can be an effective public health intervention strategy".

METHODS

Assessing Spatial Clustering within and between Periods

There are numerous methods for identifying spatial clusters, but we focus here on an adaptation of the LISA method incorporated into a fully Bayesian disease mapping model that allows for uncertainty in estimating relative risks. The benefit of such models for small areas and possibly infrequent outcomes is well established [8,9]. The literature on spatial clustering in drug related deaths includes mostly classical studies [e.g. 10, 11], though Poisson kriging has been used to for preliminary smoothing of rates [3], and empirical Bayesian methods have also been used [4,12].

Consider a variable z_i for n areas, in the form of deviations from the mean. Denote the set of areas adjacent to a particular area i as L_i (often called the spatial lag of area i), and let w_{ij} be spatial interactions which are standardised to sum to 1 over the areas within the spatial lag.

The application of the Local Indicator of Spatial Association (LISA) to spatial clustering is based on the index

$$I_i = z_i \sum_{j \in L_i} w_{ij} z_j$$

The corresponding global statistic is the Moran I apart from a scaling factor; see Anselin [13]. High-high clusters are identified when both the area risk z_i and the weighted average risk in the spatial lag area, $\sum_{j \in L_i} w_{ij} z_j$, are decisively elevated compared to other areas. More specifically, in a Bayesian estimation context via repeated MCMC sampling from the posterior, there is a high probability (e.g. 0.95) that sampled values of both z_i and $\sum_{j \in L_i} w_{ij} z_j$, are above a relevant threshold (see below) in repeated sampling. One can then say that there is a high posterior probability of a high-high risk cluster. Low-low clusters can be defined analogously. As mentioned by Anselin et al [14], the areas so identified can be regarded as the core of a cluster, where the cluster consists of both the core and neighbours, and where some clusters may be partially overlapping.

In Bayesian disease mapping models, a major focus is identifying elevated relative risks of disease, denoted ρ_i, which are latent unobservables. The typical disease mapping model has disease totals y_i, and Poisson likelihood with means $\rho_i E_i$, where E_i are expected deaths obtained by applying a standard schedule of age-specific rates to small area populations [15]. If $\sum_i y_i = \sum_i E_i$ then the average relative risk $\bar{\rho}$, is typically close to 1. The LISA calculation (incorporated into such a model) would then focus on measures $z_i = \rho_i - \bar{\rho}$, where average relative risks $\bar{\rho}$, would be calculated at each MCMC iteration from the 1279 modelled relative risks. Possibly 1 could be used as the threshold rather than $\bar{\rho}$, , so that $z_i = \rho_i - 1$.

Taking the mean relative risk as the threshold, a high-high cluster centre would be defined by a high probability (e.g. 0.9 or 0.95) both that z_i exceeds 0, and that the spatial lag average $z_i \sum_{j \in L_i} w_{ij} z_j$ exceeds 0. These exceedance probabilities can be obtained by estimation over a collection of MCMC samples, in an analogous way to that used in calculating probabilities of excess relative risk [15, page 1020]. This means that estimation of clustering probabilities takes account of uncertainty in

the outcomes, unlike classical applications which generally take outcomes as known, albeit possibly with some kind of preliminary smoothing.

The major interest here is in (a) identifying high-high and low-low clusters in any period and in (b) identifying areas which are persistent clusters between periods. With regards to clusters in a single period, four cluster types can be identified: high-high, low-low, high-low, and low-high, with other areas forming a residual unclassified group. The high-low and low-high cluster types are generally infrequent and typified as outlier cluster patterns. With MCMC sampling we can estimate within period probabilities $P_{HH,i}$ and $P_{LL,i}$ of high-high and low-low clusters, and set a high exceedance threshold such as $P_{HH,i} > 0.95$ to define those areas which can be regarded as providing high evidence of being a high-high cluster.

Estimates of these probabilities are obtained as averages over a large number of MCMC iterations of specific indicators. Let $z_i^{(t)} = \rho^{(t)} - \bar{\rho}^{(t)}$ be modelled and centred relative risks at MCMC sample t for area i. Then estimating the probability $P_{HH,i}$ involves monitoring binary indicators

$$K_{HH,i}\{ z_i^{(t)} > 0, \Sigma_{j \in L_i} w_{ij} z_j^{(t)} > 0 \}$$

where $K_{HH}(a,b) = 1$ if conditions a and b both hold, and 0 otherwise. Estimating $P_{LL,i}$ involves monitoring binary indicators

$$K_{LL,i}\{ z_i^{(t)} < 0, \Sigma_{j \in L_i} w_{ij} z_j^{(t)} < 0 \}$$

Analogously, to assess cluster persistence with MCMC methods, we can estimate probabilities

$P_{HH,HH,12i}$ (1)

that area i is a high-high cluster at both periods 1 and 2, and probabilities

$P_{LL,LL,12i}$ (2)

that an area is a low-low cluster areas in two successive periods.

Let $z_{1i}^{(t)}$ be modelled relative risks at MCMC sample t for area i and period 1, and $z_{2i}^{(t)}$ the corresponding risks for period 2. Then estimating the probability (1) involves monitoring binary indicators

$$K_{HH,HH,12i}\{ z_{1i}^{(t)} > 0, \Sigma_{j \in L_i} w_{ij} z_{1j}^{(t)} > 0 , z_{2i}^{(t)} > 0, \Sigma_{j \in L_i} w_{ij} z_{2j}^{(t)} > 0 \}$$

where $K_{HH,HH,12}i(a,b,c,d) = 1$ if all four elements (a,b,c,d) are true, and 0 otherwise. The interest would be in areas where probabilities of cluster persistence are highest, such as $P_{HH,HH,12i} > 0.95$ We can cumulate over areas to obtain totals, such as $n_{HH,HH,12}$ of areas with $P_{HH,HH,12i} > 0.95$, and $n_{LL,LL,12}$ of areas with $P_{HH,HH,12i} > 0.95$.

Note that an inter-period shift from LL to HH cluster status (or vice versa) is technically possible, as are the shift patterns (HL,HH), (HL,LL), (LH,HH) or (LH,LL). In the analysis below, none of these six shifts types occurred.

The extent of cluster persistence can be summarized by comparing persistent high-high (HH,HH) and low-low (LL,LL) totals with total HH and LL clusters in the second period. This gives measures of high-high cluster persistence and of low-low cluster persistence, namely $n_{HH,HH,12}/n_{HH,2}$ and $n_{LL,LL,12}/n_{LL,2}$.

We can also cross-classify cluster types by various socio-economic indicators for the zones. Below we cross classify $n_{HH,HH,12}$ totals, and within period totals of high-high and low-low risk, by weekly income deciles. Thus the 1279 zones are formed into decile groups using 2014 estimates (by zone) of median weekly household income before housing costs. The lowest decile contains the 10% of intermediate zones with the lowest incomes, while the highest decile contains the 10% of zones with the highest incomes.

Under a Bayesian approach, cluster persistence detection is linked with (conditional on) a particular joint likelihood model for disease risk. This model might include covariates relevant to assessing impacts of an intervention over time, or modelling the impact of particular socioeconomic characteristics such as persistent area deprivation.

Disease Risk Model

A Bayesian estimation strategy for the joint likelihood is adopted, with estimation using the WINBUGS package [16]. We assume Poisson distributed outcomes (totals of drug related deaths in the two periods), $y_{it} \sim \text{Poisson}(E_{it}\rho_{it})$ for zones i=1,..,N, and periods t=1,..,T, where N=1279, and T=2. The E_{it} denote expected event totals, obtained by applying Scotland-wide age and period specific outcome rates to zone populations. The ρ_{it} denote unknown relative risks in the two periods.

Log-link regressions for the relative risks in each period have the form

$\log(\rho_{it}) = \alpha_t + X_i\beta_t + s_{it}$, (3)

where α_t are intercepts, β_t are period specific regression parameters for p predictors $X_{i1}=(X_{i1},X_{i2},\ldots,X_{ip})$, and the S_{it} are random effects as discussed below. In this study, the predictors are defined on a [0,1] scale so their impacts can be compared. Thus if the original scores for, say, deprivation, are denoted U, the score on a [0,1] scale is obtained as $X_i = (U_i - \min(U))/(\max(U) - \min(U))$, with a scaled score of 1 for the zone with the maximum U score.

The log-link regression means that the relative risk is estimated as $\exp(\alpha_t + X_i\beta_t + s_{it})$. So assume, for illustrative purposes, that p=3 and the estimated regression coefficients are $\beta_{t1}=3.2$, $\beta_{t2}=1.2$, and $\beta_{t3}=-0.25$; that $X_{i1}=0.3$, $X_{i2}=0.2$, and $X_{i3}=0.8$; and that $s_{it}=-0.2$ and $\alpha_t=-2.4$. Then the estimated relative risk would be $\exp(-2.4+3.2\times0.3+1.2\times0.2-0.25\times0.8-0.2)=0.2$.

The S_{it} in (3) are area-period random effects which allow for spatial correlation in residual effects but do not assume all residual variability is spatially structured. They follow a bivariate extension of the Leroux et al [17,18] scheme which allows the data to determine the appropriate mix between spatial or unstructured dependence.

Let $S_i=(s_{i1},s_{i2})$, and let $S_{[i]}=(S_1,\ldots,S_{i-1},S_{i+1},\ldots,S_n)$ denote the set of bivariate effects excluding S_i. Then for the spatial

mix parameter $\xi \in [0,1]$, a 2x2 dispersion matrix Φ^{-1}, and binary spatial interactions w_{ij} (=1 for adjacent intermediate zones,=0 otherwise) the conditional mean and precision are respectively

$$E(sit|S[i]) = \xi \sum_{k \neq i} w_{ik} s_{kt} / [1 - \xi + \xi \sum_{k \neq i} w_{ik}]$$

$$Prec(S_i|S_{[i-1]}) = [1 - \xi + \xi \sum_{k \neq i} w_{ik}]^{\Phi}.$$

As ξ tends to zero, this prior density tends towards a bivariate normal without any spatial dependence, while as ξ tends to 1, the density tends towards the scheme of Mardia [19], which attributes all residual variability to spatial dependence.

The same approach can be applied to continuous variables such as social indicators hit (e.g. deprivation scores) for areas i=1,..,N and periods t=1,...,T. In the analysis of this paper we seek to estimate the extent of persistent poverty clustering in the two periods using the Scottish Government deprivation scores (SIMD) for 2012 and 2016 for the 1279 intermediate zones. A joint normal likelihood $w_{it} \sim N(_{\mu it}, \sigma^2, _t)$ (i=1,..,1279; t=1,2) is applied to standardised measures of deprivation $w_{it} = (h_{it} - \bar{h}_t)/sd_t(h))$ in the two periods, where deprivation is measured positively (higher scores for higher deprivation). Means for zone i and year t are represented as

$$\mu_{it} = \gamma_t + u_{it},$$

where γ_t are intercepts, and the spatial errors (u_{i1}, u_{i2}) are again represented by a bivariate Leroux model.

Then one can repeat the spatial cluster detection procedure described above for disease or mortality rates, but with high values based on whether centred μ_{it} exceed 0. The aim is to detect zones where probabilities of spatial cluster persistence (in deprivation) are highest, namely $P_{HH,HH,12i} > 0.95$, where the subscript HH here denotes high deprivation zones surrounded by other high deprivation zones. We can then assess overlap between persistent drug death clusters and persistent poverty clusters.

DATA: OUTCOME MORTALITY VARIABLE AND AREA RISK FACTORS

Outcome Mortality Variable:

Definitions and Background

Drug related deaths for intermediate zones during 2014-18 and 2009-13 are defined as in [5]. They were obtained by request from the Scottish General Register Office. Drug related deaths are for underlying causes defined by International Classification of Diseases,

Ninth and Tenth Revisions (ICD-9 and ICD-10) codes, as below:

As to drug types involved, most drug-related deaths involve use of more than one substance (i.e. poly-drug use), and such multiple use increases the chance of an overdose [20, 21]. The majority of deaths involve opiates such as heroin or methadone (contributing to 92% of DRDs in 2018). However, the most common pattern in drug deaths involves a combination of opiates and benzodiazepines. An example of the latter is etizolam, which contributed to 548 deaths in 2018. High-risk opioid users may use benzodiazepines to increase the effects of heroin or methadone. Drug and alcohol misuse may also be combined [20].

Area Risk Factors

The Bayesian smoothing model used to detect clusters includes area-based risk factors for drug deaths. Regarding the choice of observed covariates, many studies show strong associations between drug-related mortality and area poverty. These associations are partly compositional, due to socio-demographic differences in population structure. However, they may also reflect contextual (place) effects per se, for example, economic insecurity and place-level downward mobility [22,23].

The analysis below uses the 2016 Scotland Index of Multiple Deprivation (or SIMD) as a poverty measure, converted to be a positive measure of deprivation, and with values in [0,1]. As mentioned above, suppose the original deprivation scores are denoted U, then the score on a [0,1] scale is obtained as $X_{i1} = (Ui - min(U))/(max(U) - min(U))$, with a scaled score 1 for the zone with the highest U value. Details of the SIMD derivation are set out at https://www2.gov.scot/Topics/Statistics/SIMD, and the scores are based on seven "domains" relevant to

DESCRIPTION	ICD-9 CODES	ICD-10 CODES
Mental and behavioural disorders due to drug use	292, 304, 305.2–305.9	F11–F16, F18–F19
Accidental poisoning by drugs, medicaments and biological substances Intentional self-poisoning by drugs, medicaments and biological substances	E850–E858 E950.0–E950.5 E962.0	X40–X44 X60–X64 X85
Poisoning by drugs, medicaments and biological substances, undetermined intent	E980.0–E980.5	Y10–Y14

FIGURE 1. Shows the resulting estimated relative risks in 2014-18

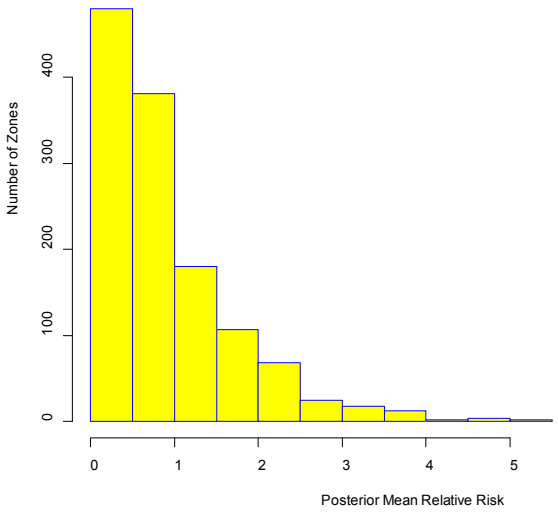


TABLE 1. Impacts Of Area Risk Factors (Posterior Mean and 95% Credible Intervals). Regression Coefficients αt and βt in Equation [3]).

2009-13	**Mean**	**2.5%**	**97.5%**
Intercept	-2.00	-2.25	-1.74
Deprivation	2.98	2.73	3.22
Fragmentation	0.85	0.55	1.14
Rurality	-0.62	-0.87	-0.39
2014-18	**Mean**	**2.5%**	**97.5%**
Intercept	-2.43	-2.58	-2.21
Deprivation	3.18	2.99	3.36
Fragmentation	1.15	0.90	1.40
Rurality	-0.29	-0.49	-0.10

poverty, such as income, housing, crime and education levels. These data inputs use both non-census data, such as welfare benefit uptake and crime levels, and Census 2011 data, such as rates of household overcrowding.

Many studies have also confirmed impacts of the social environment on drug deaths, such as an association with social cohesion, often identified as an upstream contextual influence [24]. We use an index of social fragmentation [25] as an inverse cohesion measure. The index is derived from a principal component analysis of four Census 2011 variables for the 1279 zones (percentages of one person households, adults over 15 not married, private sector renting, migration within the previous year). Scores on the first component score, which accounts for 68% of the variation in these indicators, are scaled to values in [0,1]. This index is higher in transient areas with high residential turnover [26], high numbers of non-family and one person households, above average numbers of non-married adults, and high private sector renting. In the UK, private sector renting is typically an insecure, short-stay form of housing, with surveys showing private renters less likely to trust neighbours [27]. Low scores for this index occur in areas with a more family-oriented structure, and with less residential turnover, and with more owned housing.

We also consider the impact of urbanity. The official NRS report for drug deaths in 2018 [5] shows highest DRD rates in cities such as Glasgow. The urban-rural contrast may be interrelated with that of deprivation, generally higher in Scottish cities. Rural areas such as Dumfries and Galloway, the Western Islands and Scottish Borders may have deprived pockets with high DRD rates, but their overall rate is much lower than the cities. Rurality is summarised using a ridit score, developed by Bross [28,29], applied to the ordered eight category Scottish Government Urban Rural Classification [30]. This classification ranges from a first, least rural, category, namely large urban areas, to a last (most rural) category, very remote rural. So higher ridit scores pertain to the most rural intermediate zones.

TABLE 2. Clustering Totals, Persistent and Within Period

(A) PERSISTING CLUSTER TOTALS 2014-18		
2009-13	**HH**	**LL**
HH	123	0
LL	0	322
(B) CLUSTER TOTALS WITHIN PERIODS		
2014-18	HH	141
	LL	382
	HL	23
	LH	49
2009-13	HH	140
	LL	380
	HL	14
	LH	41

Note that the ridit score is, by definition, on a [0,1] scale, and a preliminary transformation of scores is not needed. One might anticipate a negative effect of rurality on drug deaths, as urban settings and urban physical environments may affect levels of drug abuse and drug deaths [31, 21], e.g. by facilitating access to drugs.

These three area risk factors are assumed to be of equal status as covariates, albeit in an ecological study [32], with none being regarded as the central exposure, and none being regarded as confounders to any central relationship.

RESULTS

We monitor indicators of persistent high-high and low-low clustering between 2009-13 and 2014-18. Inferences are based on the second halves of MCMC runs involving two chains and 10,000 iterations, with convergence during the first 5000 iterations assessed using Brooks-Gelman-Rubin diagnostics [33]. Posterior predictive checks are based on the mixed replicate strategy of Marshall and Spiegelhalter [34], based on sampling replicate $S_i=(s_{i1},s_{i2})$.

We show firstly the effects on the risk of drug related death of the three predictors in Table 1, with the mathematical operation of coefficients to estimate relative risk as discussed above in Methods. Specifically Table 1 contains the regression coefficients from equation (3). The Table shows that the impacts of deprivation and fragmentation outweigh those of rurality in both periods, with the negative effect of rurality diminished in the later period. Nevertheless all effects are significant, in the sense that the 95% credible intervals all exclude the value zero.

The histogram in Figure 1 shows the resulting estimated relative risks in 2014-18, and the positive skew associated with high relative risks. A relatively small number of zones have high risks: 131 zones have relative risks of 2 or over, and these are especially zones with high deprivation, reflecting the elevated β coefficient for deprivation. The average deprivation score in these 131 zones is 0.89, compared to an average of 0.56 in the remaining zones.

Table 2 shows the totals of cluster types in each period (part b), and the total areas which form persistent high-high and low-low clusters between the two periods (part a). These totals are based on an exceedance threshold of 0.95. There are no areas which shift cluster status from HH to LL or vice versa between the two periods. The above suggested measures of high-high and low-low cluster persistence, namely $n_{HH,HH,12}/n_{HH,2}$ and $n_{LL,LL,12}/n_{LL,2}$, are respectively 0.87 and 0.84.

Tables 3 and 4 consider differentiation of cluster type by urbanity and by area socio-economic status. Table 3 provides an urban-rural perspective on cluster types within and between periods using the Scottish Government's eight urban-rural categories [30]. Table 3(A) shows that high-high clusters in both periods are heavily concentrated in large urban areas: 85% in 2009-13, and 82% in 2014-18. Table 3(B) shows persistent high risk clustering is also heavily concentrated in large urban areas, with 85% of persistent high risk clusters being in large urban areas. Persistent low risk clusters risk are, by contrast, spread across the eight urban-rural categories.

Table 4 shows how within and between period cluster types are distributed according to small area deprivation and fragmentation deciles, where higher deciles represent higher poverty and fragmentation. Also shown are cluster totals according to weekly income deciles (see Methods).

This Table shows that persistent high-high drug death clusters are concentrated in the highest deciles for deprivation and fragmentation, and in the lowest income decile: the average weekly income for persistent high-high clusters is

TABLE 3. Cluster Distribution of Zones by Urban-Rural Category, Within and Between Periods (a) Within Periods

2014-18 CLUSTER TYPE

	HH	LL	HL	LH	Unclassified	Total
Large Urban Areas	116	74	7	34	181	412
Other Urban Areas	25	94	15	12	333	479
Accessible Small Towns	0	52	0	1	66	119
Remote Small Towns	0	6	0	0	24	30
Very Remote Small Towns	0	2	0	0	15	17
Accessible Rural Areas	0	95	0	2	43	140
Remote Rural Areas	0	33	1	0	4	38
Very Remote Rural Areas	0	26	0	0	18	44
All categories	141	382	23	49	684	1279

2009-13 CLUSTER TYPE

	HH	LL	HL	LH	Unclassified	Total
Large Urban Areas	119	62	3	30	198	412
Other Urban Areas	21	88	11	8	351	479
Accessible Small Towns	0	58	0	1	60	119
Remote Small Towns	0	7	0	0	23	30
Very Remote Small Towns	0	2	0	0	15	17
Accessible Rural Areas	0	99	0	2	39	140
Remote Rural Areas	0	32	0	0	6	38
Very Remote Rural Areas	0	32	0	0	12	44
All categories	140	380	14	41	704	1279

(B) ACROSS PERIODS CLUSTER PERSISTENCE TYPE

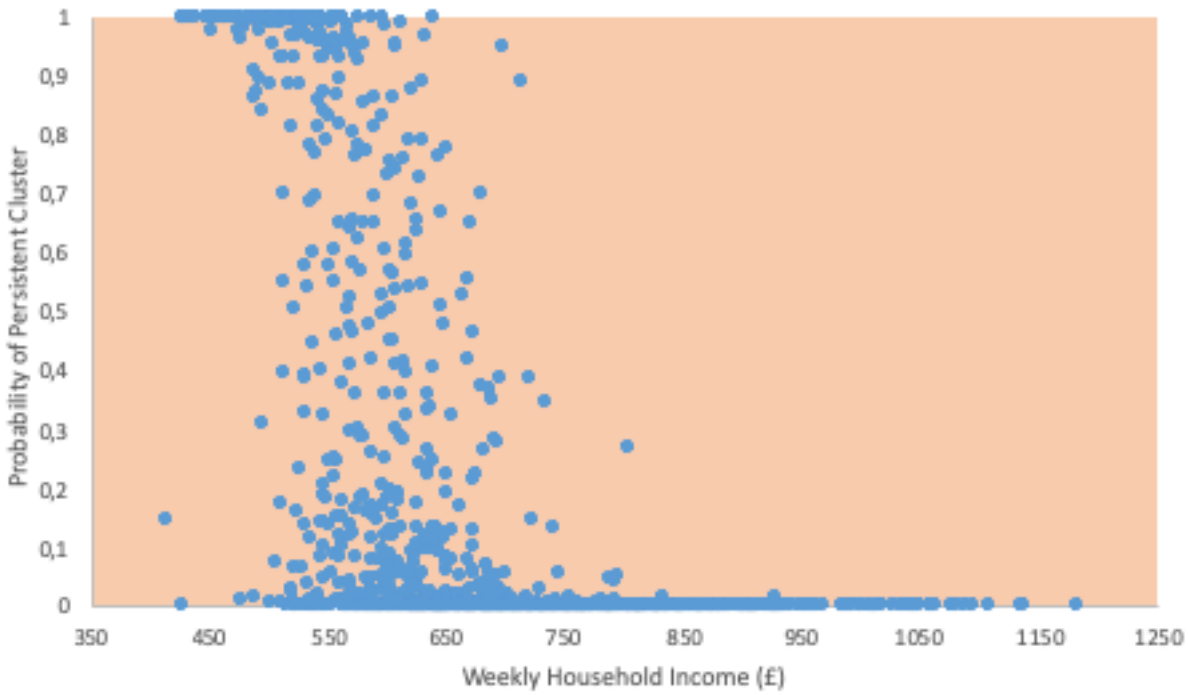
	HH-HH	LL-LL	Unclassified	Total		
Large Urban Areas	105	61	246	412		
Other Urban Areas	18	70	391	479		
Accessible Small Towns	0	45	74	119		
Remote Small Towns	0	5	25	30		
Very Remote Small Towns	0	2	15	17		
Accessible Rural Areas	0	91	49	140		
Remote Rural Areas	0	28	10	38		
Very Remote Rural Areas	0	20	24	44		
All categories	123	322	834	1279		

£515, as compared to £801 for persistent low-low clusters.

Figure 2 plots out the exceedance probabilities $P_{HH,HH,12i}$ for persistent high drug mortality clusters against weekly household incomes for zones. It shows that zones with high probabilities of persistent high-high drug mortality generally have low incomes: the average weekly income over all zones is £682.

Table 5 considers the overlap between persistent drug death and poverty clustering. There are 244 zones (of 1279) with persistent poverty clustering at the 0.95 exceedance level. Of these, 113 are also zones showing persistent high DRD clustering. So there is a 92% overlap between the two types of spatio-temporal clustering, with only 10 persisting drug mortality clusters not also forming persistent poverty clusters.

FIGURE 2. Drd cluster persistence probabilities and weekly incomes (intermediate zones)



In Scotland local authorities work together with other agencies to develop local strategies for tackling drug misuse. Table 6 accordingly shows numbers of persisting high drug death clusters by local authority, with probabilities of persisting risk exceeding 0.95. Also shown are the numbers of deprived zones in each local authority (in deciles 8 or above on the 2016 SIMD).

DISCUSSION AND CONCLUSIONS

There are increasing concerns regarding upward trends in drug-related deaths in some developed societies. Scotland is distinctive in the growth in such deaths over the last decade, a more than doubling, exceeding that in the US. One aspect of this trend is spatial concentration (clustering) in high levels of drug related deaths. This paper has investigated spatial clustering of drug deaths in Scottish small areas using fully Bayesian techniques in conjunction with local Moran measures, and has focussed especially on persistent spatial clustering.

In this regard, several studies show interplay between poverty clustering, poverty persistence, and other spatial processes, including crime, economic structure and health. Pluci-ski et al [35] consider coupled epidemiological and economic processes as the source of clusters of poverty and disease that stably persist in populations, while Rae [36] uses statistical methods to establish persistent spatial concentration of deprivation in English cities. Temporal persistence in spatial clustering of drug deaths and excess mortality may therefore be anticipated, for example, in view of spatial poverty concentration and persistence on the one hand, and strong links between drug deaths and poverty shown by many studies. However, there are relatively few relevant studies.

The above analysis shows most spatial clustering in drug related mortality in Scottish intermediate zones is persistent over two five year sub-periods in the decade 2009-18 (see Table 2). Spatial persistence in high risk clustering in this particular application is also distinct in terms of its strong association with area poverty and deprivation. In terms of regression effects, Table 1 shows a strong impact of deprivation on relative risks of drug deaths, with the impact greater in 2014-18, when drug death totals are notably higher than in 2009-13. Figure 1 shows the concentration of higher relative risks in a relatively small number of deprived zones.

However, Table 1 suggests the impact of deprivation may be moderated by differences in area social fragmentation – a negative index of social cohesion. The positive coefficient in Table 1 for fragmentation implies a negative impact of cohesion, i.e. more cohesive neighbourhoods, even deprived ones, have lower relative risks of drug related mortality than less cohesive neighbourhoods. Rurality (a negative index of urbanity) has a negative effect on drug related mortality. This implies that urbanity, and features of the urban environment, tend to enhance drug misuse and drug related deaths even after taking account of urban deprivation [21,31].

Spatial persistence in high risk clustering in this particular

TABLE 4. Cluster Types by Socioeconomic Characteristics

	2009-13 Clusters		2014-18 Clusters		Cluster Persistence Category	
Deprivation Decile. Decile 10=Highest	**HH**	**LL**	**HH**	**LL**	**HH-HH**	**LL-LL**
1	0	86	0	90	0	83
2	0	81	0	82	0	70
3	0	74	0	74	0	68
4	0	70	0	63	0	58
5	1	41	3	46	0	28
6	0	25	2	23	0	13
7	9	3	10	4	9	2
8	11	0	9	0	8	0
9	35	0	35	0	30	0
10	84	0	82	0	76	0
Totals	140	380	141	382	123	322
	2009-13 Clusters		**2014-18 Clusters**		**Cluster Persistence Category**	
Fragmentation Decile. Decile 10=Highest.	**HH**	**LL**	**HH**	**LL**	**HH-HH**	**LL-LL**
1	0	80	0	85	0	76
2	0	74	0	78	0	67
3	0	64	0	62	0	50
4	1	48	1	46	1	38
5	1	36	2	30	1	28
6	1	36	1	31	0	28
7	14	19	14	23	10	16
8	31	10	29	12	28	8
9	49	5	47	5	43	4
10	43	8	47	10	40	7
Totals	140	380	141	382	123	322
	2009-13 Clusters		**2014-18 Clusters**		**Cluster Persistence Category**	
Decile Weekly Gross Household Income (2014 Est). Decile 1=lowest incomes	**HH**	**LL**	**HH**	**LL**	**HH-HH**	**LL-LL**
1	93	1	89	1	85	1
2	32	1	36	1	28	1
3	7	9	7	7	5	6
4	6	15	6	14	3	11
5	1	34	1	30	1	22
6	0	28	0	25	0	20
7	1	59	2	58	1	47
8	0	63	0	68	0	51
9	0	68	0	74	0	65
10	0	102	0	104	0	98
Totals	140	380	141	382	123	322

TABLE 5. Drug Death Persistent Clusters and Persistent Poverty Clusters

	Persistent Drug Death Clusters	Other Zones	Total
Persistent Poverty Clusters	113	131	244
Other Zones	10	1025	1035
Total	123	1156	1279

TABLE 6. Persistent Drug Mortality Clusters by Local Authority

Local Authority	Total Number of Zones	Persistent Drug Mortality Clusters	Number of Zones in SIMD Deciles 8 and above	Ratio of Persistent Drug Mortality Clusters to Deprived Zones
Aberdeen City	49	6	10	0.60
Aberdeenshire	59	0	4	0
Angus	26	0	3	0
Argyll and Bute	23	0	2	0
City of Edinburgh	111	5	31	0.16
Clackmannanshire	12	0	4	0
Dumfries & Galloway	40	0	7	0
Dundee City	31	15	16	0.94
East Ayrshire	30	0	15	0
East Dunbartonshire	28	0	3	0
East Lothian	22	0	4	0
East Renfrewshire	20	0	2	0
Falkirk	42	0	10	0
Fife	104	6	32	0.19
Glasgow City	136	65	88	0.74
Highland	56	0	4	0
Inverclyde	17	3	7	0.43
Midlothian	22	0	6	0
Moray	24	0	0	0
Na h-Eileanan Siar	9	0	1	0
North Ayrshire	38	6	18	0.33
North Lanarkshire	78	0	41	0
Orkney Islands	6	0	0	0
Perth and Kinross	35	0	4	0
Renfrewshire	38	8	14	0.57
Scottish Borders	30	0	4	0
Shetland Islands	7	0	0	0
South Ayrshire	25	3	6	0.50
South Lanarkshire	82	4	23	0.17
Stirling	24	0	4	0
West Dunbartonshire	18	2	11	0.18
West Lothian	37	0	10	0
Total (Scotland)	1279	123	384	0.32

application is distinct in terms of its strong association with urbanity. More specifically, Table 3 shows that high-high clusters in both periods are heavily concentrated in large urban areas, as is persistent high risk clustering: 85% of persistent high risk clusters are in large urban areas.

Table 4 shows that persistent high-high drug death clusters are also concentrated in the highest deciles for deprivation and fragmentation, and in the lowest income decile. Figure 2 shows that zones with high probabilities of persistent high-high drug mortality generally have low incomes. However, not all low income areas are persistent drug mortality clusters, again suggesting moderating influences (counteracting the effect of poverty) in some areas.

In this study we also find a strong overlap between persistent drug death clustering and persistent poverty clustering. 113 of 123 zones showing persistent high DRD clustering also show persistent poverty clustering, so there is a 92% overlap between the two types of spatio-temporal clustering.

Regarding variations in drug death clustering between health agencies, we find (Table 6) that these clusters are highly concentrated in terms of local authorities affected. Of 136 zones in Glasgow, over 56 are persistent high risk clusters for drug related deaths. In Dundee, 12 of 31 zones are persistent high risk clusters, and these zones account for 73% of all drug deaths in Dundee. Also apparent is wide variation between health agencies in the relationship between numbers of deprived zones each contains, and the number of zones showing persistent drug death clustering. This may indicate varying impacts of drug related public health interventions [1], or possibly geographic variations in resilience, linked, for example, to modifying impacts of area social cohesion [24,37]. Hence, we find that social fragmentation has a significantly positive effect on drug mortality (see Table 1) even after allowing for the impact of deprivation.

Clustering in drug deaths has implications for other health outcomes often used as indices of health inequalities, including spatial inequalities, that are used to prioritize health interventions. Research has established how drug deaths contribute to increases in premature mortality [2,38,39] and to reductions in life expectancy [40]. Drug related deaths can be seen as resulting from a form of self-harm, and have been combined with suicides and alcohol related deaths in a composite outcome, labelled as "deaths of despair", increases in which have been linked to recent stagnation or falls in life expectancy in the US [41, 42].

Of particular relevance to Scotland is recent research showing that recent years have seen the slowest growth in life expectancy in Scotland since at least the 1970s, and revealing that death rates have started rising in deprived areas of the country [43,44]. The contribution of drug deaths to these trends at a national level has been recognised [45], but the role of drug deaths in spatial variation in adverse mortality trends has yet to be fully researched. The role of persistently high drug mortality as a contributor to small area mortality trends, especially in deprived areas, is potentially important in efforts by health agencies to tackle adverse mortality trends.

The main conclusions of this study can be summarised as follows. First, most spatial clustering in high risks of drug related deaths in Scotland is persistent between two sub-periods of 2009-18. High-risk clustering and persistent clustering in drug deaths show strong associations with area deprivation and with urban locations. The impact of poverty also shows clearly when persisting poverty clustering is considered. However, the impact of urban poverty on high risk clustering of drug deaths may be lessened by social cohesion, as measured inversely by social fragmentation. Regarding implications, there is scope for research on the linkages at small area level between persistent clustering in drug deaths and the location of areas with relatively low life expectancy and high premature death rates.

Competing interest statement:

None

Funding:

No specific funding received

References

1. National Aids Trust (2019) Drug-related deaths in England: local authorities and how they are responding. NAT, London
2. Shiels, M, de González, A, Best, A, Chen, Y, Chernyavskiy, P, Hartge, P, Thomas, D (2019) Premature mortality from all causes and drug poisonings in the USA according to socioeconomic status and rurality: an analysis of death certificate data by county from 2000–15. The Lancet Public Health, 4(2), e97-e106.
3. Kerry, R., Goovaerts, P., Vowles, M., Ingram, B. (2016). Spatial analysis of drug poisoning deaths in the American West, particularly Utah. International Journal of Drug Policy, 33, 44-55.
4. Rossen, L. M., Khan, D., & Warner, M. (2014) Hot spots in mortality from drug poisoning in the United States, 2007–2009. Health and Place, 26, 14-20.
5. National Records of Scotland (2019) Drug-related Deaths in Scotland in 2018. NRS, Edinburgh, Scotland
6. Laohasiriwong, W., Puttanapong, N, Luenam, A. (2017) A comparison of spatial heterogeneity with local cluster detection methods for chronic respiratory diseases in Thailand. F1000Research, 2017; 6: 1819. doi: 10.12688/f1000research.12128.2
7. Mclafferty, S. (2015). Disease cluster detection methods: recent developments and public health implications. Annals of GIS, 21(2), 127-133.
8. Mollié, A (2000). Bayesian mapping of Hodgkin's disease in France. In: Spatial Epidemiology: Methods and Applications, OUP, New York, 267-285
9. Colonna, M., Sauleau, E (2013). How to interpret and choose a Bayesian spatial model and a Poisson regression model in the context of describing small area cancer risks variations. Revue d'epidemiologie et de sante publique, 61(6), 559-567.

10. Wilt, G. E., Lewis, B, Adams, E (2019) A Spatial Exploration of Changes in Drug Overdose Mortality in the United States, 2000–2016. Preventing Chronic Disease, 2019;16:180405. DOI: http://dx.doi.org/10.5888/pcd16.180405
11. Chen, X., Wang, Y., Yu, X., Schoenfeld, E., Saltz, M., Saltz, J, Wang, F. (2017) Large-scale analysis of opioid poisoning related hospital visits in New York state. In AMIA Annual Symposium proceedings (Vol. 2017, p. 545-554). American Medical Informatics Association.
12. Stewart, K., Cao, Y., Hsu, M. H., Artigiani, E., Wish, E. (2017). Geospatial analysis of drug poisoning deaths involving heroin in the USA, 2000–2014. Journal of Urban Health, 94(4), 572-586.
13. Anselin, L. (1995) Local indicators of spatial association, LISA. Geographical Analysis, 27, 93-115.
14. Anselin L, Syabri I, Kho Y. GeoDa: an introduction to spatial data analysis. Geographical Analysis 2006; 38:5–22.
15. Richardson, S., Thomson, A., Best, N., Elliott, P. (2004) Interpreting posterior relative risk estimates in disease-mapping studies. Environmental health perspectives, 112(9), 1016-1025.
16. Lunn, D., Spiegelhalter, D., Thomas, A, Best, N. (2009) The BUGS project: Evolution, critique and future directions. Statistics in Medicine 28: 3049–3082.
17. Leroux B, Lei X, Breslow N (1999) Estimation of Disease Rates in Small Areas: A New Mixed Model for Spatial Dependence. In M Halloran, D Berry (eds.), Statistical Models in Epidemiology, the Environment and Clinical Trials, pp. 135-178. Springer-Verlag, New York
18. MacNab, Y (2007) Mapping disability-adjusted life years: a Bayesian hierarchical model framework for burden of disease and injury assessment. Statistics in Medicine, 26(26), 4746-4769.
19. Mardia, K (1988). Multi-dimensional multivariate Gaussian Markov random fields with application to image processing. Journal of Multivariate Analysis, 24(2), 265-284.
20. McPhee, I., Sheridan, B., O'Rawe, S. (2019). Time to look beyond ageing as a factor? Alternative explanations for the continuing rise in drug related deaths in Scotland. Drugs and Alcohol Today, 19(2), 72-85
21. Ompad, D., Fuller, C. (2005). The urban environment, drug use, and health. pp. 127-154 in Handbook of Urban Health, eds. Galea, S and Vlahov D. Springer, Boston, MA.
22. Monnat, S (2017) Deaths of Despair from the Cities to the Hollers: Explaining Spatial Differences in US Drug, Alcohol, and Suicide Mortality Rates. PAA Conference,
23. Knapp, E, Bilal, U, Dean, L, Lazo, M., Celentano, D (2019). Economic insecurity and deaths of despair in US counties. American Journal of Epidemiology (forthcoming). https://doi.org/10.1093/aje/kwz103
24. Dasgupta, N., Beletsky, L., & Ciccarone, D. (2018). Opioid crisis: no easy fix to its social and economic determinants. American Journal of Public Health, 108(2), 182-186
25. Congdon, P (1996) The incidence of suicide and parasuicide: a small area study, Urban Studies, 33, 137-158
26. Livingston, M., Whyte, B., Walsh, D., Bailey, N. (2013) Investigating the impact of the spatial distribution of deprivation on health outcomes. Research Report, Glasgow Centre for Population Health, University of Glasgow.
27. Swales, K.; Tipping, S. Fragmented Communities? The Role of Cohesion, Community Involvement and Social Mixing. NatCen Social Research: London, UK, 2018
28. Bross, I (1958) How to use ridit analysis, Biometrics, 14 (1):18-38
29. Chen, H, Wang, N (2014) The assignment of scores procedure for ordinal categorical data. The Scientific World Journal, 2014: 304213.
30. Scottish Government (2019) Defining Scotland by Rurality https://www2.gov.scot/Topics/Statistics/About/Methodology/UrbanRuralClassification. Accessed 15-10-2019
31. Barnum, J. D., Campbell, W. L., Trocchio, S., Caplan, J, Kennedy, L (2017) Examining the environmental characteristics of drug dealing locations. Crime & Delinquency, 63(13), 1731-1756.
32. McLaren, L., Hawe, P. (2005). Ecological perspectives in health research. Journal of Epidemiology & Community Health, 59(1), 6-14.
33. Brooks S, Gelman A (1998) General methods for monitoring convergence of iterative simulations. J Comp Graph Stat 1998; 7: 434–455.
34. Marshall, E, Spiegelhalter, D (2007) Identifying outliers in Bayesian hierarchical models: a simulation-based approach. Bayesian Analysis, 2(2), 409-444.
35. Pluci-ski, M, Ngonghala, C, Getz, W, Bonds, M (2013). Clusters of poverty and disease emerge from feedbacks on an epidemiological network. Journal of The Royal Society Interface, 10(80), 20120656.
36. Rae, A. (2012). Spatially concentrated deprivation in England: An empirical assessment. Regional Studies, 46(9), 1183-1199
37. Zoorob, M, Salemi, J (2017) Bowling alone, dying together: the role of social capital in mitigating the drug overdose epidemic in the United States. Drug and Alcohol Dependence, 173, 1-9.
38. Chen, Y., Shiels, M. S., Thomas, D., Freedman, N. D., de González, A. B. (2019). Premature mortality from drug overdoses: A comparative analysis of 13 organisation for economic co-operation and development member countries with high-quality death certificate data, 2001 to 2015. Annals of Internal Medicine, 170(5), 352-354.
39. Dibben, C (2009) One-third of the excess death rate in 15-54 year olds in Scotland due to problem drug use. Evidence-based Mental Health, 12(2), 42-42.
40. Xibiao, Y., Jenny, S., Bonnie, H., Mark, T., William, K (2018) At-a-glance-Impact of drug overdose-related deaths on life expectancy at birth in British Columbia. Health Promotion and Chronic Disease Prevention in Canada: Research, Policy and Practice, 38(6), 248
41. Muennig P, Reynolds M, Fink D, Zafari Z, Geronimus A (2018). America's declining well-being, health, and life expectancy: not just a white problem. American Journal of Public Health 108 (12), 1626-1631.
42. Woolf, S, Schoomaker, H. (2019) Life expectancy and mortality rates in the United States, 1959-2017. JAMA, 322(20), 1996-2016.
43. Fenton, L., Minton, J., Ramsay, J., Kaye-Bardgett, M., Fischbacher, C., Wyper, G, McCartney, G. (2019). Recent adverse mortality trends in Scotland: comparison with other high-income countries. BMJ Open, 9(10), doi: 10.1136/bmjopen-2019-029936
44. Fenton, L., Wyper, G, McCartney, G., Minton, J. (2019) Socioeconomic inequality in recent adverse all-cause mortality trends in Scotland. J Epidemiol Community Health, 73(10), 971-974
45. National Records of Scotland (2019) National Life Tables for Scotland 2016-2018. NRS, Edinburgh.